Amendment Dated: February 18, 2008 Reply to Office Action of October 16, 2007

<u>Amendments to the Claims:</u> This listing of claims will replace all prior versions, and listings, of claims in the application.

## Listing of Claims:

- (Currently Amended) A particle comprising a complex formed by comprising a
  bioactive agent and a complexing agent, provided that the bioactive agent is other than a
  polynucleotide and or an oligonucleotide, and wherein the particle has a bioactive
  function conferred by the bioactive agent.
- 2. (Original) The particle of claim 1, wherein the bioactive agent and/or the complexing agent have a net positive charge or have a positively charged region of at least +6.
- 3. (**Currently Amended**) The particle of claim 1, wherein the bioactive agent has the <u>a</u> net positive charge or the <u>a</u> positively charged region of at least +6 and the complexing agent has the <u>a</u> net negative charge or the <u>a</u> negatively charged region of at least -6.
- 4. (**Currently Amended**) The particle of claim ± 2, wherein the net positive charge is conferred by at least six amino acids selected from the group consisting of lysine, arginine, and histidine.
- (Currently Amended) The particle of claim 2, wherein the positively charged region of the bioactive agent is a heparin binding domain.
- 6. (Currently Amended) The particle of claim 2, wherein the other of the bioactive agent and the complexing agent has a net negative charge or has a negatively charged region of at least -6 when the complexing agent has a net positive charge or has a positively charged region of at least +6, or the complexing agent has a net negative charge or has a negatively charged region of at least -6 when the bioactive agent has a net positive charge or has a positively charged region of at least +6.
- 7. (Original) The particle of claim 1, wherein the particle has a diameter from about 1 nm to about 1000 microns.
- 8. (**Currently Amended**) The particle of claim 1, wherein the bioactive agent is a member selected from the group consisting of a growth factor, [[a]] hormone, [[a]] peptide, [[a]] protein, and or polysaccharide.
- 9. (Original) The particle of claim 1, wherein the bioactive agent is a growth factor.
- 10. (**Currently Amended**) The particle of claim  $\pm 9$ , wherein the growth factor is VEGF, PDGF, FGF, bFGF, or HGH.
- 11. (**Currently Amended**) The particle of claim 1, wherein the bioactive agent is at least one of VEGF and or PDGF.
- 12. (**Currently Amended**) The particle of claim 1, wherein the bioactive agent is a member selected from the group consisting of insulin, erythropoietin, bone morphogenic proteins, human growth hormone, human chorionic gonadotrophin, polysaccharides, transferrin,

Amendment Dated: February 18, 2008 Reply to Office Action of October 16, 2007

TGF-beta receptors, integrin heterodimer receptor,  $\underline{or}$  Fas-L<sub>7</sub> and receptor fragments for FGF, PDGF, VEGF, and CAR.

- 13. (**Currently Amended**) The particle of claim 1, wherein the complexing agent is a polysaccharide, glycosaminoglycan, complex carbohydrate, or polyacid member selected from the group consisting of polysaccharides, glycosaminoglycans, complex carbohydrates, polyacids, modifications and derivatives thereof.
- 14. (**Currently Amended**) The particle of claim 1, wherein the complexing agent is a member selected from the group consisting of dextran, dextran sulfate, chitosan, heparin, heparan, heparan sulfate, hyaluronic acid, chondroitin, chondroitin sulfate, dermatan sufate, keratan sulfate, pentasan sulfate, alginate, and carageenan, polyglutamic acid, and or 3-polyphosphoric acid.
- 15. (Original) The particle of claim 14, wherein the complexing agent is dextran or dextran sulfate having a molecular weight of about 2 KDa to about 10,000 KDa.
- 16. (Original) The particle of claim 15, wherein the molecular weight of dextran or dextran sulfate is from 5 KDa to 500 KDa.
- 17. (Original) The particle of claim 1, wherein the particle is free of poly(ethyleneimine).
- 18. (Withdrawn) The particle of claim 1, further comprising an agent, wherein the agent is a member selected from the group consisting of an antibody, an antigen, a receptor, and a ligand.
- 19. (**Currently Amended**) The particle of claim 1, further comprising a matrix, wherein the complex is contained within a matrix is associated with at least one of the bioactive agent and the complexing agent.
- 20. (**Currently Amended**) The particle of claim 19, wherein the matrix is a <u>biodegradable polymer</u>, colloidal particle, liposome, emulsion, solid particle, magnetic particle, protein, or polypeptide member selected from the group consisting of biodegradable polymers, colloidal particles, liposomes, emulsions, solid particles, magnetic particles, proteins, and peptides.
- 21. (Original) The particle of claim 20, wherein the particle is free of poly(ethyleneimine).
- 22. (Original) The particle of claim 1, wherein the particle is completely biodegradable.
- 23. (Original) The particle of claim 1, wherein the particle comprises at least 40% of the bioactive agent.
- 24. (Original) The particle of claim 1, wherein the particle comprises from about 40% to about 90% of the bioactive agent.
- 25. (Original) The particle of claim 1, wherein the particle consists essentially of the bioactive agent and the complexing agent.

Amendment Dated: February 18, 2008 Reply to Office Action of October 16, 2007

- 26. (**Currently Amended**) A particle comprising a complex formed by comprising a bioactive agent and a complexing agent, wherein one of the bioactive agent and the complexing agent is a cationic agent or an anionic agent having a net charge or a region having a net charge of at least 6 units and wherein the particle has a bioactive function conferred by the bioactive agent.
- 27. (Original) The particle of claim 26, wherein the bioactive agent is the cationic agent and the complexing agent is the anionic agent.
- 28. (**Currently Amended**) The particle of claim <del>26</del> <u>27</u>, wherein the cationic agent is <del>a member selected from the group consisting of</del> a growth factor, [[a]] hormone, [[a]] peptide, [[a]] protein, and or polysaccharide.
- 29. (Original) The particle of claim 28, wherein the cationic agent is a growth factor.
- 30. (Original) The particle of claim 29, wherein the growth factor is VEGF, PDGF, FGF, bFGF, or HGH.
- 31. (**Currently Amended**) The particle of claim ± 27, wherein the cationic agent is at least one of VEGF and or PDGF.
- 32. (**Currently Amended**) The particle of claim <del>26</del>-<u>27</u>, wherein the anionic agent is a <u>polysaccharide, glycosaminoglycan, complex carbohydrate, or polyacid</u> <del>member selected from the group consisting of polysaccharides, glycosaminoglycans, complex carbohydrates, polyacids, modifications and derivatives thereof.</del>
- 33. (**Currently Amended**) The particle of claim <del>26</del> <u>27</u>, wherein the anionic agent is <del>a member selected from the group consisting of dextran, dextran sulfate, chitosan, heparin, heparan, heparan sulfate, hyaluronic acid, chondroitin, chondroitin sulfate, dermatan sufate, keratan sulfate, pentasan sulfate, alginate, <del>and</del> carageenan, polyglutamic acid, and or 3-polyphosphoric acid.</del>
- 34. (**Currently Amended**) The particle of claim 31 33, wherein the anionic agent is is dextran or dextran sulfate having has a molecular weight of about 2 KDa to about 10,000 KDa.
- 35. (Original) The particle of claim 26, wherein the particle is free of poly(ethyleneimine).
- 36. (Original) A particle consisting essentially of a complex between a growth factor and a polysaccharide.
- 37. (Withdrawn) A method of making the particle of claim 1, the method comprising: providing a bioactive agent; providing a complexing agent; and mixing the bioactive agent and the complexing agent at a pH of about 1 to about 13 to form the complex between the bioactive agent and the complexing agent, provided that the bioactive agent and the complexing agent are structural parts of the complex, and thereby making the particle.
- 38. (Withdrawn) The method of claim 37, wherein the pH is from 4.5 to 7.5.

Amendment Dated: February 18, 2008 Reply to Office Action of October 16, 2007

- 39. (Withdrawn) The method of claim 37, wherein the complex is formed by an electrostatic interaction between the bioactive agent and the complexing agent.
- 40. (Withdrawn) The method of claim 37, wherein mixing is conducted in a low ionic strength buffer.
- 41. (Withdrawn) The method of claim 40, wherein the buffer is an MES buffer.
- 42. (Withdrawn) The method of claim 37, further comprising a stabilizing agent selected from the group consisting of mono and disaccharides.
- 43. (Withdrawn) The method of claim 40, wherein the stabilizing agent is selected from the group consisting of glucose, monose, trehalose, glycerol, and albumin.
- 44. (Withdrawn) The method of claim 37, further comprising providing at least one of a matrix and an agent.
- 45. (Withdrawn) The method of claim 37, wherein the matrix is a member selected from the group consisting of biodegradable polymers, colloidal particles, liposomes, emulsions, solid particles, magnetic particles, proteins, and peptides and wherein the agent is a member selected from the group consisting of an antibody, an antigen, a receptor, and a ligand.
- 46. (Withdrawn) A method of administering of the particle of claim 1, comprising: providing the particle, wherein the particle is adapted to gradually release the bioactive agent; and administering the particle to a cell by at least one of a parenteral, an inhalation or an oral route.
- 47. (Withdrawn) The method of claim 46, wherein administering is done by the parenteral route.
- 48. (New) The particle of claim 36, wherein the growth factor is VEGF or PDGF.
- (New) A particle comprising a complex of a growth factor and dextran, dextran sulfate, chitosan, heparin, heparan, heparan sulfate, hyaluronic acid, chondroitin, chondroitin sulfate, dermatan sufate, keratan sulfate, pentasan sulfate, alginate, carageenan, polyglutamic acid, or 3-polyphosphoric acid.
- 50. (New) The particle of claim 49, wherein the growth factor is VEGF or PDGF.
- (New) A particle comprising a complex of erythropoietin and dextran, dextran sulfate, chitosan, heparin, heparan, heparan sulfate, hyaluronic acid, chondroitin, chondroitin sulfate, dermatan sufate, keratan sulfate, pentasan sulfate, alginate, carageenan, polyglutamic acid, or 3-polyphosphoric acid.